

Amendments to the Specification

Please replace paragraph [0007] with the following amended paragraph inserting sequence listing identifiers:

[0007] In one aspect, the invention provides a peptide including the sequence: Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro. (SEQ. ID. NO. 1)

Please replace paragraph [0008] with the following amended paragraph inserting sequence listing identifiers:

[0008] In another aspect, the invention provides a peptide including the sequence: Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser. (SEQ. ID. NO. 2)

Please replace paragraph [0009] with the following amended paragraph inserting sequence listing identifiers:

[0009] In another aspect, the invention provides a peptide including the sequence: Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe-Val-Leu-Asp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr. (SEQ. ID. NO. 3)

Please replace paragraph [0010] with the following amended paragraph inserting sequence listing identifiers:

[0010] As described herein, the inventors have found that peptides including the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1) have a certain functional activity that is characterised by a capacity to inhibit growth of *M. canis*, *M. gypseum*, *T. tonsurans*, *T. rubrum* and *T. mentagrophytes*. This is believed to be the first demonstration of peptides of this class that have antifungal activity against these fungal pathogens.

Please replace paragraph [0013] with the following amended paragraph inserting sequence listing identifiers:

[0013] The inventors recognise that a peptide that includes a sequence that, but for one or more amino acid residues, is essentially the same as the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro, would be expected to have a capacity to inhibit growth of these fungal pathogens. These peptides could be made according to the processes described further herein. The capacity of these peptides to inhibit growth of fungi that cause or are otherwise associated with tinea, such as *M. canis*, *M. gypseum*, *T. tonsurans*, *T. rubrum* and *T. mentagrophytes*, could be determined by the assays described further herein. In view of the above, it will be understood that the invention includes peptides that have an amino acid sequence that is homologous to the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro or an amino acid sequence that is homologous to the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser (SEQ. ID. NO. 2) or an amino acid sequence that is homologous to the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe-Val-Leu-A- sp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr (SEQ. ID. NO. 3). These peptides are referred to as "variants". Further to amino acid sequence homology with either Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro, (SEQ. ID. NO. 1) Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser (SEQ. ID. NO. 2) or Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe-Val-Leu-A- sp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr (SEQ. ID. NO. 3), the variants are characterised in terms of a capacity to inhibit growth of fungi that cause or are otherwise associated with tinea, such as *M. canis*, *M. gypseum*, *T. tonsurans*, *T. rubrum* and *T. mentagrophytes*, as determined by the assays described herein.

Please replace paragraph [0014] with the following amended paragraph inserting sequence listing identifiers:

[0014] "Homology" with respect to amino acid sequence is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the

sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1), or in the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser (SEQ. ID. NO. 2), or in the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe-- Val-Leu-Asp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr (SEQ. ID. NO. 3), after aligning the sequences and introducing gaps if necessary to achieve the maximum identity. No N- or C-terminal extension or deletion in the candidate sequence shall be construed as reducing homology.

Please replace paragraph [0015] with the following amended paragraph inserting sequence listing identifiers:

[0015] Typically a variant is a peptide that has for example, at least about 75% amino acid homology with the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1) or with the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser (SEQ. ID. NO. 2) or with the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe-- Val-Leu-Asp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr (SEQ. ID. NO. 3). The variant may have at least 80%, more typically, greater than 85% sequence homology, for example, 90% amino acid homology, with the sequence of Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1), Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser (SEQ. ID. NO. 2) or Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe-Val-Leu-A- sp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr (SEQ. ID. NO. 3). However, a variant may exhibit less than 50% sequence homology with the sequence of Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1) or Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asp-Gly-Asp-Phe-Ala-Ala-Ser (SEQ. ID. NO. 4) and still retain the characteristics of a variant as described herein.

Please replace paragraph [0016] with the following amended paragraph inserting sequence listing identifiers:

[0016] As described herein, peptides of the invention, including variants, may be prepared by chemical synthesis methodologies or by recombinant DNA technology. For example, peptides of the invention can be prepared from monomers using a chemical synthesis methodology based on the sequential addition of amino acid residues, for example as described in Merrifield, J. Am. Chem. Soc., 85: 2149 (1963). These monomers may be naturally occurring residues, or non naturally occurring residues, examples of which are described below. Alternatively, the peptides of the invention, and in particular, a variant, can be prepared by enzymatically or chemically treating a peptide including the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1). Where the peptides are to be synthesised by recombinant DNA technology, they may be prepared by random or predetermined mutation (eg site directed PCR mutagenesis) of a nucleic acid molecule that encodes an amino acid sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1), or a sequence that has homology with Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1), and expression of the sequence in a host cell to obtain the peptide. This is a particularly useful process for preparing variants. An alternative process is de novo chemical synthesis of a nucleic acid molecule that encodes Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1) or a sequence that is homologous to Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1) and expression of the sequence in the host cell to obtain the peptide.

Please replace paragraph [0017] with the following amended paragraph inserting sequence listing identifiers:

[0017] The peptides of the invention that are variants of the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1) or Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser (SEQ. ID. NO. 2) or Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe-Val-Leu-A- sp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr (SEQ. ID. NO. 3), typically differ in

terms of one or more conservative amino acid substitutions in these sequences. Examples of conservative substitutions are shown in Table 1 below.

Please replace paragraph [0018] with the following amended paragraph inserting sequence listing identifiers:

[0018] ~~Aaa~~ Xaa-Ile-Lys-Leu-Val-Gln-Ser-Pro wherein ~~Aaa~~ Xaa is Ala or Leu or Val (SEQ. ID. NO. 5);

Please replace paragraph [0019] with the following amended paragraph inserting sequence listing identifiers:

[0019] Ala-~~Bbb~~ Xaa-Lys-Leu-Val-Gln-Ser-Pro wherein ~~Bbb~~ Xaa is Leu, Ile, Pro or Val (SEQ. ID. NO. 6);

Please replace paragraph [0020] with the following amended paragraph inserting sequence listing identifiers:

[0020] Ala-Ile-~~Cee~~ Xaa-Leu-Val-Gln-Ser-Pro wherein ~~Cee~~ Xaa is Lys, Pro, Asn, Gln or His (SEQ. ID. NO. 7);

Please replace paragraph [0021] with the following amended paragraph inserting sequence listing identifiers:

[0021] Ala-Ile-Lys-~~Ddd~~ Xaa-Val-Gln-Ser-Pro wherein ~~Ddd~~ Xaa is Leu, Ile or Val (SEQ. ID. NO. 8);

Please replace paragraph [0022] with the following amended paragraph inserting sequence listing identifiers:

[0022] Ala-Ile-Lys-Leu-~~Eee~~ Xaa-Gln-Ser-Pro wherein ~~Eee~~ Xaa is Leu, Ile or Val (SEQ. ID. NO. 9);

Please replace paragraph [0023] with the following amended paragraph inserting sequence listing identifiers:

[0023] Ala-Ile-Lys-Leu-Val-~~Fff~~ Xaa-Ser-Pro wherein ~~Fff~~ Xaa is Gln, Asn, His or Lys (SEQ. ID. NO. 10); and

Please replace paragraph [0024] with the following amended paragraph inserting sequence listing identifiers:

[0024] Ala-Ile-Lys-Leu-Val-Gln-~~Ggg~~ Xaa-Pro wherein ~~Ggg~~ Xaa is Ser or Thr (SEQ. ID. NO. 11).

Please replace paragraph [0048] with the following amended paragraph inserting sequence listing identifiers:

[0048] A useful method for identification of a residue of the sequences Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1), Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser (SEQ. ID. NO. 2) and Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe-Val-Leu-A- sp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr (SEQ. ID. NO. 3) for amino acid substitution to generate a variant is called alanine scanning mutagenesis as described by Cunningham and Wells (1989) Science, 244:1081-1085. Here a residue or group of target residues are identified (eg charged residues such as Asn, Gln and Lys) and replaced by a neutral or negatively charged amino acid to affect the interaction of the amino acids with the surrounding environment. Those domains demonstrating functional sensitivity to the substitution then are refined by introducing further or other variations at or for the sites of substitution. Thus while the site for introducing an amino acid sequence variation is predetermined the nature of the mutation per se need not be predetermined. For example, to optimize the performance of a mutation at a given site, Ala scanning or random mutagenesis may be conducted at the target

codon or region and the expressed peptide screened for the optimal combination of desired activity.

Please replace paragraph [0055] with the following amended paragraph inserting sequence listing identifiers:

[0055] Fusion proteins can be made by the chemical synthesis methods describe below, or they can be made by recombinant DNA techniques, for example, wherein a nucleic acid molecule encoding the peptide having the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1), or the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser (SEQ. ID. NO. 2) or the sequence Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe--Val-Leu-Asp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr (SEQ. ID. NO. 3) is arranged in a vector with a gene encoding another protein or a fragment of another protein. Expression of the vector results in the peptide of the invention being produced as a fusion with another protein or peptide.

Please replace paragraph [0103] with the following amended paragraph inserting sequence listing identifiers:

[0103] The invention also provides a nucleic acid molecule that encodes a peptide according to the invention. Examples of these nucleic acid molecules include molecules having a nucleotide sequence selected from the group consisting of:

(i) 5'-GCU AUC AAA CUG GUU CAG UCC CCG-3' (SEQ. ID. NO. 12);

(ii) 5'-GCU AUC AAA CUG GUU CAG UCC CCG AAC GGU AAC UUC GCU GCU UCC-3' (SEQ. ID. NO. 13), and

(iii) 5'-GCU AUC AAA CUG GUU CAG UCC CCG AAC GGU AAC UUC GCU GCU UCC
UUC GUU CUG GAC GGU ACC AAA UGG AUC UUC AAA UCC AAA UAC UAC-3'
(SEQ. ID. NO. 14).

Please replace paragraph [0104] with the following amended paragraph inserting
sequence listing identifiers:

[0104] In view of the well known degeneracy of the genetic code, it will be understood that the
nucleic acid molecules of the invention may contain one or more points of nucleotide sequence
difference, and in particular, one or more codons that are different to the above described nucleic
acid molecules. Thus for example, the nucleic molecule that encodes Ala-Ile-Lys-Leu-Val-Gln-
Ser-Pro (SEQ. ID. NO. 1) may include the sequence 5'-GCA AUU AAG CUC GUA CAA UCU
CCA-3' (SEQ. ID. NO. 15), rather than 5'-GCU AUC AAA CUG GUU CAG UCC CCG-3'
(SEQ. ID. NO. 12).

Please replace paragraph [0106] with the following amended paragraph inserting
sequence listing identifiers:

[0106] The invention also provides a nucleic acid molecule including a sequence that is
complementary to the sequence of a nucleic acid molecule that encodes a peptide according to
the invention. An example of such a molecule is 3'-CGA TAG TTT GAC CAA GTC AGG
GGC-5' (SEQ. ID. NO. 16).

Please replace paragraph [0139] with the following amended paragraph inserting
sequence listing identifiers:

[0139] Peptides were considered as showing a capacity to inhibit *M. canis*, *M. gypseum*, *T.*
tonsurans, *T. rubrum* and *T. mentagrophytes* provided that the percentage inhibition observed
was greater than the control wells. The peptides Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro, Ala-Ile-Lys-

Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser (SEQ. ID. NO. 2) and Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe-Val-Leu-A- sp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr (SEQ. ID. NO. 3) showed greater than 50% and up to 97% inhibition of growth of *M. canis*, *M. gypseum*, *T. tonsurans*, *T. rubrum* and *T. mentagrophytes*.

Please replace paragraph [0142] with the following amended paragraph inserting sequence listing identifiers:

[0142] Peptides were considered as showing a capacity to inhibit *M. canis*, *M. gypseum*, *T. tonsurans*, *T. rubrum* and *T. mentagrophytes* provided that the percentage inhibition observed was greater than the control wells. The peptides Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro (SEQ. ID. NO. 1), Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser (SEQ. ID. NO. 2) and Ala-Ile-Lys-Leu-Val-Gln-Ser-Pro-Asn-Gly-Asn-Phe-Ala-Ala-Ser-Phe-Val-Leu-A- sp-Gly-Thr-Lys-Trp-Ile-Phe-Lys-Ser-Lys-Tyr-Tyr (SEQ. ID. NO. 3) showed greater than 50% and up to 97% inhibition of growth of *M. canis*, *M. gypseum*, *T. tonsurans*, *T. rubrum* and *T. mentagrophytes*.